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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,999	EGGELING ET AL.	
	Examiner	Art Unit	
	KAGNEW H. GEBREYESUS	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 1,2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *7-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☒ Claim(s) *28 and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/07/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Applicant's election with traverse dated August 01, 2008 to the restriction requirement mailed on April 10, 2008 is acknowledged. Applicants elected the invention of Group IV encompassing claim 27 and the species of SEQ ID NO: 1. Claims 28 and 29 are new.

Applicants traverse the restriction requirement on the grounds that the foreign priority document for the instant application antedates the reference used in the lack of unity of invention. This priority document was not available at the time the instant application was first filed.

Furthermore, applicants argue that:

"...the novel 3-phosphoglycerate dehydrogenases of the present invention not only have reduced feedback inhibition, but also retain strong enzymatic activity. According to the central paragraph of page 3 of the application, other prior art was known at the time the present application was filed disclosing that the C-terminal of 3-phosphoglycerate dehydrogenase of *E. coli*, not Corynebacterium glutamicum, contained the allosteric binding site for L-serine, and that if this region in the gene is completely deleted, or at least altered, that the problem of feedback inhibition may be overcome. However, the resulting modified 3-phosphoglycerate dehydrogenase has much less enzymatic activity..."

However coryneform bacteria in which the feedback inhibition of D-3-phosphoglycerate dehydrogenase activity by L-serine in view of producing L-serine was

known in the prior art. For example US 6,037,154 published for Suga et al teaches such coryneform bacteria in which the serB and serC genes were enhanced and where the feedback inhibition by serine of D-3-phosphoglycerate dehydrogenase was desensitized (see column 6, lines 42-67 and column 7 line 1-48 and claims 11 and 22). Thus the technical feature relied upon by Applicant is not a special technical feature.

However since the method of claim 27, 28 and 29 apply the nucleic acid sequences of SEQ ID NO: 1-5 and each sequence encodes an enzymatically active fragment derived from SEQ ID NO: 6, claims 1-10, 27 and 28-29 are rejoined and are present for examination. Claims 11-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claims.

Claims 28 and 29 are methods of producing L-serine which also apply the polynucleotide fragments to SEQ ID NO: 1-5, therefore I have rejoined them with claims 1-6.

Priority

This application is a national stage application of PCT/DE03/02290 filed on July 08, 2003 and claims the benefit of foreign priority from German application filed under on July 10 2002. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement filed on January 07, 2005 for which a copy

of the patent publication has been submitted in this application has been considered as shown by the Examiners signature next to each reference.

Oath/Declaration

The oath or declaration submitted on January 06, 2006 has been reviewed and is in compliance with 37 CFR 1.56.

Drawings

The drawings were received on January 07, 2005. These drawings are accepted.

Specification

This application contains sequence disclosures at pages 28 and 29 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a((1) and (a)(2). However, the fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below: Nucleic acid sequences of 10 or more nucleotides and amino acid sequences of 4 or more residues need to be designated with a sequence identifier. Wherein attention is directed to paragraph(s) §1.82 (c) and (e).

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no

new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO. Although an examination of this application on the merits can proceed without prior compliance, compliance with the Sequence Rules is required for the response to this Office action to be complete.

Claim Objections

Claims 7-27 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative form only and cannot depend from any multiple dependent claim. See MPEP § 608.01(n). Accordingly, claims 7-10 and 27 have ***not*** been further treated on the merits.

Claims 28 and 29 are objected to because of the following informalities: Claims 28 and 29 are objected because these claims recite "...translated into a Coryneform bacterium..." The term "translated into" is misused in this instance because the proper terminology in this context is: "...transformed into a Coryneform bacterium..."

In addition claim 28(a) recites ..."and selected from..." which should read "...selected from..." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and contain grammatical and idiomatic errors. For example claim 1 recites "...Nucleic acids coded for a deregulated 3-phosphoglycerate dehydrogenase containing a gene serA...**or** an allele, homolog **or** derivative of..." However a nucleic acid encodes a protein according to accepted grammatical and idiomatic expression in the art.

Claim 1-5 appears to be drawn to: "A polynucleotide sequence comprising a fragment of a serA gene wherein said fragment comprises SEQ ID NO: 1-5, an allele, homolog, derivative thereof and polynucleotides that hybridize with SEQ ID NO: 1 wherein said polynucleotides encode a feedback insensitive (deregulated) 3-phosphoglycerate dehydrogenase". Furthermore it is not clear if the allele, homolog or derivative have the desired 3-phosphoglycerate dehydrogenase activities. Furthermore the claims encompass polynucleotides that hybridize to SEQ ID NO: 1-5 where said sequences can have any size including short sequences of 10-30 nucleotides according to the specification. However these short fragments are not expected to have enzymatic activity while an allele or homolog may have activity. Thus the claims encompass embodiments with different scopes/limitations. Clarification is desired.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to a genus of polynucleotide sequences comprising fragments of SEQ ID NO: 6 (SEQ ID NO: 1-5) (with 3-phosphoglycerate dehydrogenase and any allele, homolog, derivative or any polynucleotide that hybridizes with SEQ ID NO: 1-5). Furthermore the claims are drawn to vectors comprising said genus of sequences and a method of producing L-serine in microbial cells comprising said genus of polynucleotide sequences. The specification teaches the structure of fragments of a single species consisting of SEQ ID NO: 1, 2, 3, 4 or 5 that encode the polypeptides of SEQ ID NO: 7-11 and retain variable levels of 3-phosphoglycerate dehydrogenase activity (3-PGDH activity). However, the specification fails to describe any other species by any identifying characteristics or properties for the genus of polynucleotides encompassed. This is because the specification defines "allele" as a functional equivalent with any substitution, deletion, addition or insertion (specification page 7) and defines "a homolog" as any complementary polynucleotide sequence that can hybridize with the recited fragments which include polynucleotides of any size and short fragments with 10-30 nucleotides (specification page 9).

However to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the claims do not describe other members of the genus by structure, physical and/or chemical characteristics.

Furthermore the definition of allele is so broad that it can include any number of changes (any substitution, deletion, addition, insertion etc). Furthermore any polynucleotide sequence that hybridizes under stringent condition with the polynucleotide of SEQ ID NO: 1-5 includes short sequences of 10 nucleotides or a long sequence comprising any PDGH from any source.

The specification only discloses fragments comprising SEQ ID NO: 1-5 from only one allele (SEQ ID NO: 6) within the scope of the genus wherein all of these fragments retain 3-phosphoglycerate dehydrogenase activity. The function of all other species in the genus are not disclosed, and there is no known or disclosed correlation between the unknown structures and the unknown functions (i.e. phenotypes), or between the unknown structures and the polynucleotide fragments of SEQ ID NO: 1-5.

The general knowledge in the art concerning alleles does not provide any indications of how the structure of one allele is representative of other unknown alleles having concordant or discordant functions. The common attributes of the genus are not described and the identifying attributes of alleles, other than the disclosed fragments of

SEQ ID NO: 6 are not described. Furthermore according to the definition in the specification an allele can have any substitution, deletion, addition etc thus the genus can include members that have widely divergent properties.

One skilled in the art would conclude that the applicant was not in possession of the claimed genus because a description of fragments of a single member of the genus is not representative of the variant of the genus and is insufficient to support the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,037,154 (Suga et al). Suga et al teach an L-serine production method that utilizes a coryneform bacterium that is transformed with a *ser*B and *ser*C genes involved in the pathway of L-serine biosynthesis. Furthermore in a preferred embodiment Suga teaches microorganisms further comprising a feedback insensitive 3-phosphoglycerate dehydrogenase (3-PGDH or *ser*A gene) which comprises a mutation in the gene encoding the same (see column 6, line 42-48). Coryneform bacteria comprising a mutant PDGH with one or more substitutions, deletions or additions and where the 325th glutamic acid was substituted by other amino acids such as lysine resulted in an L-serine insensitive strain (polynucleotide of SEQ ID NO: 13 encoding SEQ ID INO 14).

The instant claims are drawn to a genus of polynucleotide sequences comprising SEQ ID NO: 1-5, any allele, homolog, derivative or any polynucleotide that hybridizes thereto and vectors comprising the same (claims 1-6) and a method of producing L-serine in microbial cells comprising said genus of polynucleotide sequences in a culture media comprising carbon sources such as glucose fructose, galactose saccharified starch etc. and various nitrogen sources such as ammonia gas, solutions and ammonium salt. Furthermore Suga et al teach that organic nitrogen sources such as oil cakes, soybean hydrolysate liquid etc. further they teach that as inorganic ions, phosphoric acid can be added in the media (see column 7, lines 51-67 and column 8 lines 1-3). Furthermore Suga et al teach that the L-serine can be collected from the growth media by separating and removing the cells, subjecting to ion exchange resin treatment, concentration cooling, crystallization, membrane separation or combinations thereof for collecting the L-serine.

The specification defines "allele" as a functional equivalent with any substitution, deletion, addition or insertion (specification page 7) to SEQ ID NO: 1-5. Furthermore the specification defines "a homolog" as any complementary sequence that can hybridize with the recited fragments of SEQ ID NO: 1-5 including polynucleotides of 10-30 nucleotides (specification page 9) and any large sequence. However the polynucleotide sequence and the use of the same to produce L-serine in a microorganism disclosed in US 6,037,154 (see also claims 11 and claim 22) is within the limitation of these variant sequences. Therefore claims 1-6 are anticipated by US 6,037,154.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,258,573 (Suga et al). Suga et al teach an L-serine production method that utilizes a coryneform bacterium transformed with a feedback insensitive 3-phosphoglycerate dehydrogenase gene (3-PGDH gene or *ser*A gene) where said gene encodes a modified PGDH. Example for such an L-serine feedback insensitive (deregulated) PDGH was generated by mutating the 3-PGDH of SEQ ID NO: 12 from *Brevibacterium flavum*. Corynebactrium comprising one or more substitutions, deletions, insertion or additions, and where the 325th glutamic acid was substituted by lysine and resulted in an L-serine insensitive strain. The instant claims are drawn to a genus of polynucleotide sequences (SEQ ID NO: 1-5), any allele, homolog, derivative or any polynucleotide that hybridizes with thereto comprised in a vector and a method of producing L-serine in microbial cells comprising said genus of polynucleotide sequences.

The specification defines "allele" as a functional equivalent with any substitution, deletion, addition or insertion (specification page 7) and defines "a homolog" as any complementary sequence that can hybridize with the recited fragments of SEQ ID NO: 1-5 including polynucleotides of 10-30 nucleotides (specification page 9). Thus the polynucleotide sequence disclosed by Suga et al which comprises additional nucleotides compared to the polynucleotides of SEQ ID NO: 1-5 in the instant invention and which are feedback resistant to L-serine anticipate claims 1-6 because the polynucleotide of SEQ ID NO: 13 encoding the polypeptide of SEQ ID NO: 14 can be considered an allelic variant, a homolog or a polynucleotide that hybridizes with any of

the polynucleotides of SEQ ID NO: 1-5 of the instant invention. Thus claims 1-6 are anticipated.

Conclusion:

No claims are allowed. However, although the polynucleotide of SEQ ID NO: 6 and the encoded polypeptide of SEQ ID NO: 12 are found in the prior art, the prior art does not teach the use of the specific fragments of SEQ ID NO: 1-5 encoding the polypeptide of SEQ ID NO: 7-11 for the production of L-serine in Coryneform bacteria.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656

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